

In the Claims

Claim 1 (Withdrawn): A conditionally inducible site-directed mutant cell, comprising

- a) a mutated allele of a gene; wherein said allele comprises a mutation that was introduced by using a suitable mutagenesis technique,
- b) a rescue allele of said mutated gene that can be conditionally inactivated,

wherein said mutation in said mutated allele of said gene interferes with survival and/or causes an adverse phenotype.

Claim 2 (Withdrawn): The conditionally inducible site-directed mutant cell according to claim 1, wherein said mutated allele of said gene comprises a mutation at the exon or sub-exon level, wherein said mutation is selected from the group consisting of deletions, point mutations, insertions, and inversions.

Claim 3 (Withdrawn): The conditionally inducible site-directed mutant cell according to claim 1, wherein said rescue allele and/or its transcription product(s) comprises recombination target sites, sites for the attachment of antisense oligonucleotides, sites for ribozyme activities, and/or sites that interfere with specific siRNA for expression.

Claim 4 (Withdrawn): The conditionally inducible site-directed mutant cell according to claim 1, wherein said rescue allele comprises a conditionally inducible genetic construct which either directly or via its expression product inhibits the function of any non-mutated copy of said mutated allele.

Claim 5 (Withdrawn): The conditionally inducible site-directed mutant cell according to claim 1, containing multiple mutated alleles of genes and/or a multiply mutated allele of a gene together with their suitable rescue allele(s).

Claim 6 (Withdrawn): The conditionally inducible site-directed mutant cell according to claim 1, wherein said allele encodes titin.

Claim 7 (Withdrawn): The conditionally inducible site-directed mutant cell according to claim 1, wherein said interference with survival and/or adverse phenotype is selected from temporal and/or local phenotypes,.

Claim 8 (Withdrawn): The conditionally inducible site-directed mutant cell according to claim 1, which is selected from a prokaryotic cell, a eukaryotic cell, a diploid cell, a plant cell, a mammalian cell, a nematode cell, a fish cell, an insect cell, and a non-human stem-cell.

Claim 9 (Withdrawn): A conditionally inducible site-directed mutant cell culture, tissue, organ, non-human embryo, or non-human organism comprising a conditionally inducible site-directed mutant cell, comprising

- a) a mutated allele of a gene; wherein said allele comprises a mutation that was introduced by using a suitable mutagenesis technique,
- b) a rescue allele of said mutated gene that can be conditionally inactivated,

wherein said mutation in said mutated allele of said gene interferes with survival and/or causes an adverse phenotype.

Claim 10 (Cancelled)

Claim 11 (Withdrawn): The conditionally inducible site-directed mutant non-human organism according to claim 9, containing multiple mutated alleles of genes and/or a multiply mutated allele of a gene together with their suitable rescue allele(s).

Claim 12 (Withdrawn): The conditionally inducible site-directed mutant non-human organism according to claim 9, wherein said interference with survival and/or adverse phenotype is selected from temporal and/or local phenotypes.

Claim 13 (Currently amended): A method for producing an inducible site-directed mutant cell capable of conditional gene rescue, comprising

- a) introducing in a target cell a mutated allele of a gene to be mutated by using a suitable mutagenesis technique, and
- b) introducing in said target cell a rescue allele of said gene, wherein the rescue allele that can be conditionally inactivated; ~~and~~
- e) ~~optionally, cultivating said target cell under conditions that allow for a selection of cells that contain both the mutated allele and the rescue allele of said gene;~~

thereby producing an inducible site-directed mutant cell capable of conditional gene rescue,

wherein said mutation in said mutated allele of said gene interferes with survival and/or causes an adverse phenotype, and

wherein said suitable mutagenesis technique comprises introducing a mutation at the exon or sub-exon level that leads to a disturbed interaction of the mutated gene product with other components of the cell.

Claim 14 (Cancelled)

Claim 15 (Previously presented): The method according to claim 13, wherein introducing said rescue allele comprises transfection or infection of the cell with a rescue allele genetic construct comprising recombination target sites, sites for the attachment of antisense oligonucleotides, sites for ribozyme activities, and/or sites that interfere with specific siRNA for expression.

Claim 16 (Cancelled)

Claim 17 (Currently amended): The method according to claim 13, wherein a tissue specific rescue allele and/or tissue specific mutated allele is introduced.

Claim 18 (Currently amended): The method according to claim 13, wherein said mutated and/or rescue allele encodes titin.

Claim 19 (Previously presented): The method according to claim 13, wherein said cell is selected from a prokaryotic cell, a eukaryotic cell, a diploid cell, a plant cell, a mammalian cell, a fish cell, a nematode cell, an insect cell, and a non-human stem-cell.

Claim 20 (Previously presented): The method according to claim 13, comprising the introduction of multiple mutated alleles of genes and/or a multiply mutated allele of a gene together with their suitable rescue allele(s).

Claim 21 (Previously presented): The method according to claim 13, wherein said interference with survival and/or adverse phenotype is selected from temporal and/or local phenotypes.

Claim 22 (Currently amended): The method according to claim 13, further comprising ~~[[d]]~~ c) conditionally inactivating said rescue allele of said gene to be mutated by using a ~~suitable~~ inactivation technique.

Claim 23 (Currently amended): The method according to claim 22, wherein conditionally inactivating said rescue allele of said gene to be mutated by using a ~~suitable~~ inactivation technique comprises a technique selected from site directed recombination, antisense inactivation using oligonucleotides, RNA-interference, siRNA expression-inactivation, inactivation of the gene product (protein) and/or its activity and/or inducible inactivation of the non-mutated allele, inactivation of the activity of a fusion protein or induced proteolysis.

Claim 24 (Previously presented): The method according to claim 13, wherein said method is performed in vivo or in vitro.

Claim 25 (Previously presented): The method according to claim 13, wherein said cell is present in a tissue, organ, non-human embryo or non-human organism.

Claim 26 (Currently amended): A method for the production of an inducible site-directed non-human mutant-organism comprising a cell capable of conditional gene rescue, comprising

- a) generating an inducible site-directed mutant cell by a method comprising
 - i) introducing in a target cell a mutated allele of a gene to be mutated by using a suitable mutagenesis technique, and
 - ii) introducing in said target cell a rescue allele of said gene, wherein the rescue allele that can be conditionally inactivated, and
 - ~~— iii) optionally, cultivating said target cell under conditions that allow for a selection of cells that contain both the mutated allele and the rescue allele of said gene,~~

wherein said mutation in said mutated allele of said gene interferes with survival and/or causes an adverse phenotype; and

wherein said suitable mutagenesis technique comprises introducing a mutation at the exon or sub-exon level that leads to a disturbed interaction of the mutated gene product with other components of the cell; and

- b) generating a non-human mutant organism comprising said mutant cell.

Claim 27 (Withdrawn): An inducible site-directed non-human mutant-organism, produced according to a method comprising

- a) generating an inducible site-directed mutant cell by a method comprising
 - i) introducing in a target cell a mutated allele of a gene to be mutated by using a suitable mutagenesis technique,
 - ii) introducing in said target cell a rescue allele of said gene that can be conditionally inactivated, and
 - iii) optionally, cultivating said target cell under conditions that allow for a selection of cells that contain both the mutated allele and the rescue allele of said gene,

wherein said mutation in said mutated allele of said gene interferes with survival and/or causes an adverse phenotype; and

- b) generating a non-human mutant organism comprising said mutant cell.

Claim 28 (Withdrawn): The method, according to claim 3, wherein said rescue allele and/or its transcription product(s) comprises lox or FRT sites.

Claim 29 (Withdrawn): The method, according to claim 7, wherein said temporal and/or local phenotype is selected from the group consisting of cell cycle-specific, cell-type specific, tissue-specific, protein-expression specific, tissue-development specific, organ-specific, organ-development-specific and embryonic lethal phenotypes.

Claim 30 (Withdrawn—Currently amended): The mutant non-human organism according to claim 12 wherein said temporal and/or local phenotype is selected from the group ~~consisting~~ consisting of cell cycle-specific, cell-type specific, tissue-specific, protein-expression specific, tissue-development specific, organ-specific, organ-development-specific and embryonic lethal phenotypes.

Claim 31 (Currently amended): The method, according to claim 14, wherein said ~~suitable~~ mutagenesis technique employs a vector system, irradiation, random integration of foreign DNA, site specific recombination, homologous recombination, or chemical mutagenesis.

Claim 32 (Previously presented): The method, according to claim 21, wherein said temporal and/or local phenotype is selected from the group consisting of cell cycle-specific, cell-type specific, tissue-specific, protein-expression specific, tissue-development specific, organ-specific, organ-development-specific and embryonic lethal phenotypes.

Claim 33 (Previously presented): The method, according to claim 23, wherein said inactivation technique is selected from the group consisting of cre/lox or Flp/FRT inactivation; ribozyme activity inactivation; and inactivation of the non-mutated allele using an antibody.

Claim 34 (Previously presented): The method, according to claim 25, wherein said non-human organism is a mammal, rodent, nematode, fish, plant, or insect.

Claim 35 (New): The method, according to claim 13, which further comprises cultivating said target cell under conditions that allow for a selection of cells that contain both the mutated allele and the rescue allele of said gene.

Claim 36 (New): The method, according to claim 26, which further comprises cultivating said target cell under conditions that allow for a selection of cells that contain both the mutated allele and the rescue allele of said gene.